

# Edited Transcript of Clitoxin® Procedure Video

By Charles Runels, MD

## The Serious Problem: Sexual Dysfunction in Women

Sex problems in women can take several forms.<sup>1</sup> A woman can suffer pain (dyspareunia), she can have decreased lubrication, which can cause pain and other problems, decreased arousal, and decreased desire. She can also have trouble with orgasm, either a decrease in intensity or difficulty in having an orgasm. Any one or more of those problems can cause decreased satisfaction.

These problems do not solely decrease sexual pleasure; by definition, for a woman to warrant the diagnosis by her physician of “sexual dysfunction,” she must suffer psychological distress because of her symptoms. If she only complains of symptoms that decrease pleasure, without secondary psychological distress, she does not have sexual dysfunction.

Even by that strictest of definitions, it is still estimated around 40% of women suffer from their sex, and surprisingly, the incidence is higher *in younger* women.<sup>2</sup>

Why should younger women suffer more sex problems?

Some may guess that younger women would suffer less because they enjoy a younger body. The answer is in the definition. When a young woman (starting her family and making her first relationships) suffers dyspareunia, anorgasmia, and decreased arousal, that can be more distressing for her than for a woman who has already reared her children, or is widowed or divorced and has determined to take time to live alone.

This definition of sexual dysfunction in women is unusual among the diagnosis criteria for the disease. For example, if your blood pressure is elevated and you are not psychologically bothered by it, you still have hypertension. Or if a male has an inability to have an erection, he has erectile dysfunction, regardless of his emotions about the condition. Since the definition of female sexual dysfunction requires that she be distressed by the problem, menopausal women may still suffer symptoms (perhaps more frequently than their younger siblings), but are not counted as having sexual dysfunction because they are less likely to be as upset.

## Sexual dysfunction interferes with much more than pleasure.

As a physician, I have cared for thousands of women over the past 36 years. Many of those women told me that when they enjoy good sex and good orgasms, it increases their creativity, but when they have sex problems, they have trouble focusing, and their family relations are strained. Women often tell me they use orgasm either with a lover or masturbating to help fall asleep and deal with depression and anxiety. Sex has far-reaching effects across all parts of a woman's life.<sup>3</sup>

## It is Not Just to Please a Man

Improving sex is not about women pleasing men. Women should love themselves. Sometimes, that self-love involves another person; sometimes, it does not.

## Female Sexual Dysfunction and the Clitoxin® Procedure

An elderly woman told me, “I was sad when I had to put my wife in the nursing home because of her dementia. But I make love to myself. Why should men have all the fun? Orgasms make me happier.”

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*Better sex helps a woman love herself.*

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Still, a woman can want to bring pleasure to her lover. Imagine a man completely content with his premature ejaculation and giving no thought to the frustration of his female lover. It can be good for him to want to bring her pleasure, and it can be good for the woman to want to bring pleasure to her

husband, but it is also good for her to love herself. Sexual dysfunction can lessen all these pleasures.



## Options for Treating Sexual Dysfunction in Women

The options to treat sex problems in women include the FDA-approved drugs: flibanserin, bremelanotide, and topical DHEA.<sup>4</sup>

Other drugs have been shown by research to help with sex, but the FDA does not approve their use to help with sex—making them off-label, non-FDA-approved. For example, Wellbutrin and testosterone are commonly prescribed to help women with sex but are not FDA-approved for that purpose.<sup>5 6</sup>

Other options include lubrication, fantasy, sex counseling or family

counseling, sex toys, and the O-Shot® procedure<sup>7 8</sup>. Options also include surgery (for phimosis and other pain problems), lasers, radiofrequency, and Kegel machines<sup>9</sup>.

Lubricants do not solve most sex problems (only help with dyspareunia from dryness).

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Family counseling or sex counseling is tremendously helpful and can make almost any problem better, but counseling to facilitate acceptance of a physical problem by learning how to cope better is not the same as making the problem go away (unless the problem is psychological or social with no physical etiology).

None of those therapies are magic bullets.

None.

Not one.

For comparison, if you suffer pain, you can take morphine, and most will have less pain—almost guaranteed. You can take a sleeping pill, and you will likely fall feel sleepy.

But we do not have a counterpart in the sexual medicine arena where most people can do one thing, and they are guaranteed to enjoy better sex.

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*There is nothing for female sex problems with a guaranteed restoration to good sex.  
There are no magic bullets.*

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There are also significant side effects with our current options to help women with sex. For example, flibanserin should not be taken with alcohol because the combination can cause a dangerous drop in blood pressure.<sup>10</sup> Also, flibanserin must be taken every day, even if you do not plan to have sex that day. In the studies of flibanserin, the reward (for taking the drug every day and not drinking any alcohol) was that the woman averaged enjoying sex *one more time per month—one*.<sup>11</sup>

Not 2.

1 extra sex encounter per month.

With bremelanotide, significant nausea, often with vomiting, is a common side effect.

Vomiting usually mixes poorly with candlelight.

### Nothing for Orgasm

Even though there are three FDA-approved drugs to help women with sex, none of them are indicated to help women enjoy more or better orgasms directly.

### No Magic Bullets

So, we do not have an effective, universal treatment for female sex problems.

We have only three FDA-approved drugs to help women with sex. Two of the three approved drugs are psychiatric drugs (they only affect the brain): flibanserin and bremelanotide. The only one designed to help the genitalia of the female is DHEA cream, which is only FDA-approved to help postmenopausal women with pain.

That's it, *just three drugs approved by the FDA to help women with sex—two are psychiatric drugs, and the other is only for postmenopausal women to relieve pain, while men enjoy the option of over twenty FDA-approved sex drugs; the drugs are for men of every age; and, most of the drugs for me directly target the improvement of the function and health of the male genitalia.*

## Female Sexual Dysfunction and the Clitoxin® Procedure

Judging by our FDA-approved menu of drugs, we are telling men that we can help the function of their genitalia to help them to better sex, but with women, we are telling them, “Your sex problems are mostly in your head.”

### **The Need for *Systems Analysis* to Understand Treatment Options**

Since there are no “magic bullets” for treating sexual dysfunction in women, there must be a systems analysis to allow for optimal results (and to expand options to include additions to the psychiatric drugs).<sup>12 13 14 15</sup>

The best way to think about systems analysis is to consider someone struggling to breathe: you would not give everyone suffering shortness of breath a bronchodilator because some may not have asthma (or bronchospasm). She may be a child who aspirated a foreign body into his trachea, aspirated a penny, or a small toy.

Shortness of breath (dyspnea) can be caused by severe anemia (insufficient red blood cells are available to carry the oxygen). Dyspnea can be caused by cyanide poisoning, emphysema, a collapsed lung, or psychiatric problems (anxiety or fear).

So, you would not treat everyone suffering from dyspnea with a bronchodilator or give everyone a transfusion. Instead, you use systems analysis to diagnose which component (or components) need treatment; physicians use systems analysis daily and habitually to diagnose and treat every medical problem.

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*Physicians were taught to examine the penis, the foreskin, the testicles, and the prostate,  
but not the clitoris, the clitoral hood, or the labia minora.*

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I do not see systems analysis employed universally in treating sexual dysfunction as with other medical problems. I often see physicians, for example, buy a new device, and then almost everyone with a sex problem gets treated with that; maybe they buy a vaginal laser or something else on our list, a radiofrequency device, or a Kegel machine, or maybe they have just learned about flibanserin, and everybody gets that. Physicians are reckless most of the time; it is just that as part of their training, there has been less understanding and emphasis on systems analysis when treating female sexual problems.

Historically, when it comes to female sexual dysfunction, there's much more research regarding male sexuality, and because of that, the understanding of the female orgasm system is less thorough, and the deployment of systems analysis is subsequently less frequent.

It wasn't that long ago that the clitoris was not even drawn into the anatomy textbooks.

As physicians, we were all taught to examine the penis, the testicles, and the prostate, but not the clitoris.

I've been teaching physicians in my hands-on workshops and online for 13 years, and when I teach, I like to ask, "Were you ever taught to examine the clitoris when you were in medical school?"

So far, no one has answered “Yes” to that question.

They always answer, “No.”

## Female Sexual Dysfunction and the Clitoxin® Procedure

Research has demonstrated that the thoroughness of teaching even the anatomy of female sexuality is much less for females than for males.<sup>16</sup>

### What is a System?

Multiple components working together to accomplish a purpose make a system.<sup>17 18 19 20</sup> And there can be systems within systems. There can be a solar system; within that solar system exists the earth-moon system, where the satellite (moon) orbits the earth. The circulatory system is a component of the body system.

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*A system is multiple components working together to accomplish a purpose.*

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One component of the female orgasm system is hormones, so at least part of the endocrine system is a component of the female orgasm system.

There are also mechanical systems within the orgasm system (muscles and bones); for example, there must be a structure to the posterior vagina to push the penis against the anterior vaginal wall for stimulation of the woman. Making the vagina smaller in diameter is not just about stimulating the penis. The penis must have something supporting it, or else there's no pressure on the G-spot or the urethra or the mechanism of sensation (imagine a vagina with no posterior wall, there would be zero stimulation of the anterior vagina). So, there's a mechanical component to the female orgasm system.

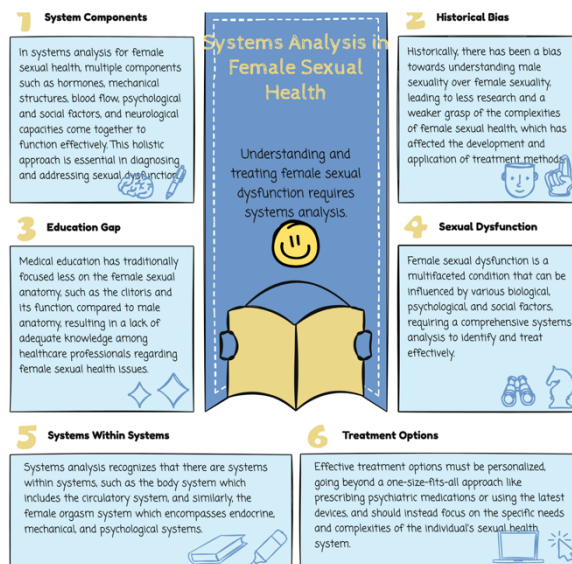
Muscle contraction and relaxation are part of the pleasure of orgasm.

Also, it is impossible to enjoy good sex without good blood flow and respiration because there is some exercise component and a blood flow component to sex.

There is a psychological component. Maybe the woman was abused, or maybe she has depression. Maybe she has compulsions that are not for her best health.

There is a social component. Perhaps her relationship is not so good, or the structure of her household is so there's no privacy or intimacy. Or perhaps she enjoys a lover who demonstrates caring and understanding of her body and emotions.

And, of course, there's a neurological component to the female orgasm system; a woman must be able to "feel" and be aware of what she is feeling.



## Female Sexual Dysfunction and the Clitoxin® Procedure

One might argue that the female orgasm system has been largely undefined because it is extremely complicated, but that offers no legitimate alibi for not defining the system and thinking deeply about how to treat the dysfunction of the system.

### The Importance of the Autonomic Nervous System

There are two **subsystems** within the nervous system component of the female orgasm system.

First, there's a *somatic nervous system*: voluntary movement and conscious sensation. If you decide to move your left hand, that's a somatic movement; that is voluntary. If you touch something with your finger or if the clitoris is touched, that is a somatic sensation.

Second is the autonomic nervous system: the part of your nervous system that tells your heart how fast to beat (without it, the heart would stop beating) and tells your bowels when to have peristalsis. *The autonomic nervous system tells you when to sweat or to shiver and when to feel aroused.* The primary arousal center in the brain is within the hypothalamus. Of course, there is communication between the midbrain (autonomic) and the cerebrum; you are aware that you're aroused, just like you're aware that you feel hot or cold when you shiver, but **it's the midbrain that is controlling that autonomic nervous system, and there are nerves corresponding to both parts (somatic and autonomic) of the neurological system.**<sup>21 22 23 24</sup>

There are the somatic nerves for conscious sensations. However, the autonomic nervous system input and output, even though less a part of consciousness, are just as powerful.

Consider the pain when someone is having a heart attack. She may have left arm pain even though the arm is not being damaged, but because the innervation and the flow of the nerves from the heart are less granular, the brain cannot tell exactly what is being damaged. It can only tell something is hurting. If

you have pain from a kidney stone, it feels like a severe backache with nausea; your brain does not tell you that there is swelling in your ureter. So, there's less granularity with the autonomic nervous system, but it is still very important, perhaps more important than the somatic nervous system in some ways because it governs all body functions.

Shut off the somatic nerves to your hand—that is disturbing. Shut off the autonomic nervous system—you die.

And you would lose all sexual desire.

Considering the current body of research, the autonomic nervous system (sympathetic and parasympathetic) that controls and regulates

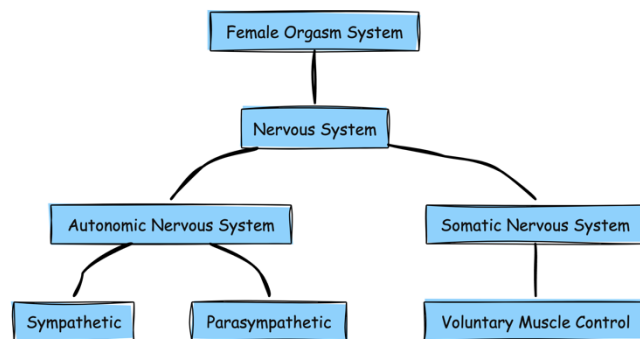


Figure 1. The nervous system is one of the subcomponents of the female orgasm system. The nervous system contains the subcomponents of the autonomic and the somatic nervous system.

the female sexual response has been relatively ignored.<sup>23</sup> There is no malintent. It has not been discussed or studied as much as the male autonomic nervous system in relation to sex.

For example, by the time most finish college and by the time everybody finishes medical school, people know that the parasympathetic part of the autonomic nervous system, which has to do with relaxation (versus the sympathetic part, which has to do with the fight-or-flight response) has the most to do with erection in men. But even most physicians have a vague understanding of the function of the autonomic nervous system in females during the sexual response. There have been, thankfully, some heroic efforts



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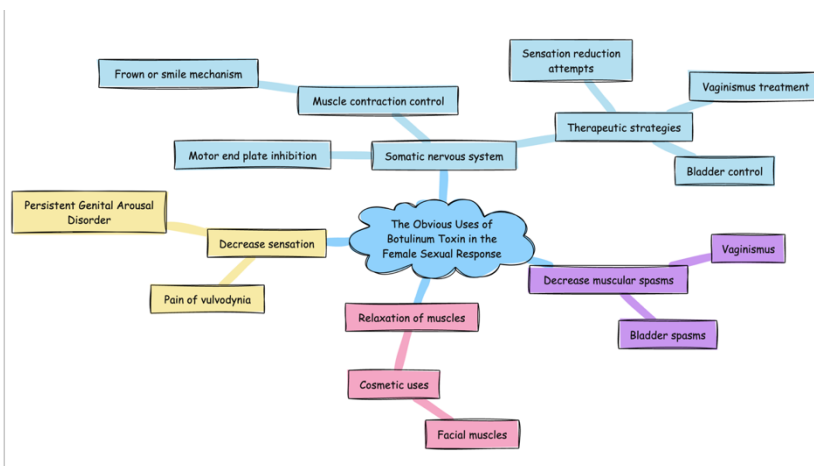
to correct that mismatch of research and understanding. One recent study showed, for example, what happens to the autonomic nerves when a mid-urethral sling is placed, which is a legitimate and needed surgical procedure.<sup>25</sup> But if you're paying attention to the somatic nerves of the clitoris and not to the autonomic nerves, then harm becomes more likely.

## The Obvious Uses of Botulinum Toxin in the Female Sexual Response

Botulinum toxin (BoNT) has been injected for over a decade to decrease unwanted and painful muscle contraction, or spasms, of the vagina (vaginismus)<sup>26 27</sup> and to relax bladder spasms.<sup>28 29</sup> It's also been used to attempt to *decrease* sensation, not quite as successfully, for the pain of vulvodynia<sup>30 31</sup> and the misery of unwanted, *persistent genital arousal disorder*.<sup>32</sup> In both areas, decreasing muscle contraction and decreasing sensation, botulinum toxin strategies have involved mostly thinking about the somatic nervous system. That's also how it's used cosmetically: you inject it into the muscles of the face; it interferes with the motor end plate or the communication of the nerve with the muscle, and the muscle relaxes.

That is a somatic nerve response.

You can frown or smile, and the muscle moves. Botulinum toxin interferes with that communication and



causes relaxation. In the same way, it's thought to work with vaginismus and bladder spasms. And there's been an attempt to, again, decrease nerve signal transmission with persistent genital arousal disorder and vaginismus.

## The Not-Obvious Effect of BoNT When Injected

But if you go to the migraine arena, here's a clue to something not obvious about how botulinum toxin might help in the female with sex. It was thought at one time that botulinum toxin helped relieve migraines by just relaxing the muscles. Although that is true with bruxism, where there's a spasm of the masseter muscle that causes teeth to clench, relaxing the muscle does help the resultant headaches.<sup>33 34</sup> But with true migraine headaches, it is now thought that relaxing the muscles of the face is not how botulinum toxin works to decrease the frequency and intensity of migraines.

It is now postulated, and research has demonstrated that botulinum toxin, when you inject the face (for example, in the procerus muscle between the eyes), migrates along the axon by being brought into the Schwann cell (endocytosis), and then the botulinum toxin travels along the nerve until it *reaches the ganglion*.<sup>35 36 37</sup>

I'll say that again: *You inject the muscle of the face, but the way it helps with migraines is not by relaxing the muscle. BoNT helps with migraines because it goes along the nerve to the switchboard mechanism called a ganglion, and the ganglion then connects to another nerve that goes to the brain. That ganglion, the trigeminal ganglion, is where the nerve connects from the procerus muscle. The trigeminal ganglion*

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and the caudate nucleus are also shared by the same nerves that come from the pain fibers in the meninges, and that's where the pain starts with migraine.

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*BoNT has been primarily used to treat the somatic nervous system component of the female orgasm system.*

*Because it also affects the autonomic nervous system, BoNT effects when injected in the clitoris were not obvious.*

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*You're using the muscle of the face as a port to inject the ganglion switchboard, shared by the nerves coming from the meninges, and, therefore, block the pain of migraine.*

You are not treating migraine by relaxing the muscle injected; that idea is a clue to how botulinum toxin might work in a very non-obvious way to help female sexuality.

### **The Unexpected Result When BoNT is Injected**

When you think about the somatic nervous system and the female sexual response, you think about the pudendal nerve, which goes to the dorsal nerve of the clitoris. In other words, that's where you consciously feel the sensation when the clitoris is stimulated or touched. It travels along the dorsal nerve, and that's a somatic response.<sup>38</sup> One might postulate that putting botulinum toxin in the clitoris might worsen the sexual response by blocking nerve transmission.

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*Because BoNT injected into the clitoris primarily affects the autonomic nervous system (not the somatic nervous system), the results are opposite and unexpected from what previous uses of BoNT would predict.*

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But when considering the non-obvious component, the autonomic nervous system, and how botulinum toxin could migrate along the nerves of the autonomic nervous system that connect to the midbrain, the hypothalamus (where the arousal center lies), then you have an understanding of the possibility of *unexpected results: that botulinum toxin would not decrease the response, either sensation or muscle contraction, but rather increase arousal by heightening the baseline level of the arousal center*. So, that mechanism is not obvious if you're thinking about the somatic nerves (which is what most have thought about regarding female sexual response), and if the results were to improve sex, that would be unexpected but would be explained by the autonomic response.

### **Clitoxin®: a Specific Method for Injecting the Clitoris with Botulinum Toxin to Improve Sex for Women.**

To test for the unexpected results of the non-obvious, my wife and I did a study where we looked at what happened when women wanted improvement in their sexuality, and they had either failed or did not want the current therapies.<sup>39</sup>

When they chose to experience the injection of botulinum toxin into the clitoris, we postulated that it might work in three different ways: (1) by affecting the autonomic nervous system, as I described, (2) by

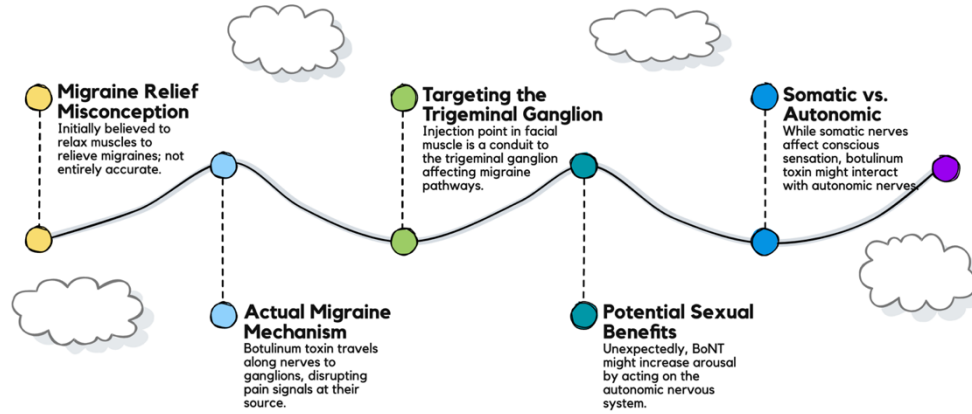


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increasing arterial blood flow by relaxing the muscles that control blood flow to the clitoris, and (3) by triggering the regeneration of healthier tissues.

**BONT's Surprising Migraine & Sexuality Effects**

Botulinum toxin addresses migraines and may enhance female arousal via nerve pathways to the ganglion to affect the autonomic nervous system.



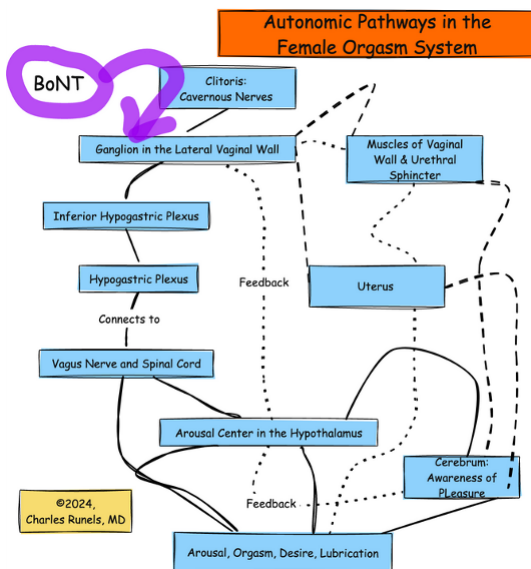
**1. Activation of the Autonomic Nervous System**

“BoNT” stands for botulinum neurotoxin, which could be any brand name. We used Xeomin® in our study for the reasons described in our research.<sup>39</sup>

After injecting the clitoris with

botulinum toxin, if it then behaved as it does with migraine treatment,<sup>36</sup> traveling from the facial muscles to the trigeminal ganglion to the caudate nucleus to affect the autonomic nervous system, then, after injection into the clitoris, BoNT would travel to the ganglion in the lateral vaginal wall through the cavernous nerves—which would then signal the arousal center.

With the dorsal nerve of the clitoris, a woman consciously feels her clitoris. However, there are nerves in the clitoris that are not sensation nerves.<sup>40 25</sup> In other words, when you inject the clitoris, the brain is consciously aware of sensation through the dorsal nerve of the clitoris, but it's the midbrain, the non-



conscious brain, the same brain that is keeping track of your bowels and your heart and your sweating and your shivering—that brain is also connected to the clitoris through the cavernous nerves, which then go out of the clitoris into the lateral vaginal wall to the ganglia. That’s the parasympathetic part of the autonomic nervous system.

The sympathetic nervous system takes a different route, but both (sympathetic and parasympathetic) connect to ganglia (switchboards), which, when affected by BoNT, change the set point of those ganglia.<sup>41</sup>

Then, that signal from the ganglia goes through the inferior hypogastric plexus or the splenic plexus to the spinal cord and then to the arousal center of the hypothalamus.

And then you have feedback loops because when the hypothalamus, the arousal center says, "Oh, there is a change..." Just like with migraines, there's been a change; although the clitoris isn't being stimulated, the baseline arousal level is raised by the botulinum toxin affecting the ganglion.

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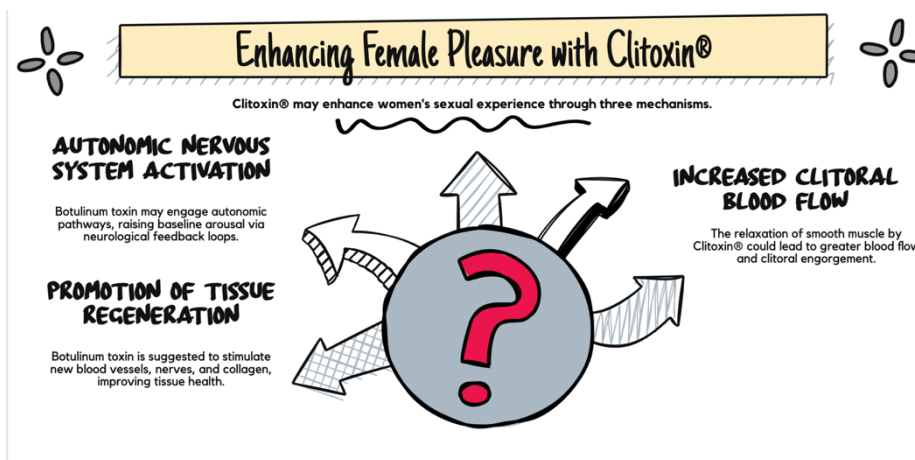
So, the arousal center in the hypothalamus says, "Oh! We're at a more aroused state," and it may not be all the way to persistent genital arousal (where she's just got to have sex right now), but it might make her more easily aroused.

Then, the cerebrum becomes aware of that feeling and may seek pleasure, sexual relationships, or self-love because the arousal center is becoming more heightened, or because the arousal center is more heightened, there may be an easier transition from non-aroused to arousal. Then, when that feedback happens, the lateral hypothalamus tells the cerebrum to be more aroused but feeds back through the same autonomic nerves to the genitalia to increase pleasure. The signals go in both directions—traveling through afferent nerves (going back to the brain) and efferent nerves (leaving the brain). When signals leave the brain, they might tell the vagina to lubricate, and when orgasm happens, it may tell the uterus and the vagina to contract. So, feedback loops are happening with this positive spiral that leads to better sex. At least, that's what we thought might happen.

### 2. Botulinum toxin relaxes smooth muscle to increase blood flow to the clitoris.

Botulinum toxin also relaxes smooth muscle. This has been known for over a decade. That's why it's used to relax the bladder in women with bladder spasms to help with incontinence.<sup>42 43</sup> Arterioles within the clitoris have smooth muscles that line the wall, making them smaller in diameter when those muscles contract.

When they relax, the diameter is larger, so more blood can flow through. It could be that the botulinum toxin might relax the muscles of the arterioles, leading to more blood flow and increased engorgement of the clitoris, which could cause increased stimulation.



### 3. Botulinum toxin triggers tissue regeneration.

Other effects of botulinum toxin that have been known since the 1950s are that it can stimulate the growth of new blood vessels, nerves, and collagen. A lot of this research happened in the study of healing surgical wounds.<sup>44 45 46 47 48 49 50</sup>

For example, injecting the tissue with botulinum toxin blocks the motor end plate, but then the Schwann cell adapts by growing new neurons or nerves to adapt to that blocking. So, you have new nerves, and in the same way, you can see neovascularization and collagenesis. So, there are three ways that botulinum toxin could help. It might help by affecting the autonomic nervous system, increasing arterial blood flow, and triggering the regeneration of healthier tissue. But all that was a postulate until we did the study that we'll talk about momentarily.

## What Is Not Possible with the Clitoxin® Procedure?

Before we talk about the results of our study, I want to re-emphasize that there are no magic shots. You can't fix a low testosterone level or a high prolactin level from a micro-adenoma with an injection of botulinum toxin into the clitoris, and an elevated prolactin level is very likely to cause decreased desire and possibly anorgasmia. If a woman suffers from a uterine fibroid that's causing pain, that's not going to get better with an injection of the clitoris, just like you can't make shortness of breath caused by anemia better by giving someone a bronchodilator.

In other words, for the best diagnosis and treatment, you must think about the whole orgasm system and decide what might be helpful using that systems analysis, just like you would with the respiratory system, the cardiovascular system, the lymphatic system, the gastrointestinal system, or any other system. Those posters were put on the wall in your schoolroom in the fifth grade to help you understand how components work together, all at the same time, with positive and negative feedback loops, to create an outcome.

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*There are no magic shots.*

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So if the woman has suffered prior sexual abuse, if she's in a toxic relationship, has not dealt with those problems, or if she has a lover who doesn't understand her body and they are not matching in the bedroom, then she will be made all happy from just injecting botulinum toxin in her clitoris.

And in our study, the treatment seemed less helpful for postmenopausal and not hormonally replaced. It was also not as helpful for pain, although we did see that it significantly increased lubrication, arousal, orgasm, and satisfaction.

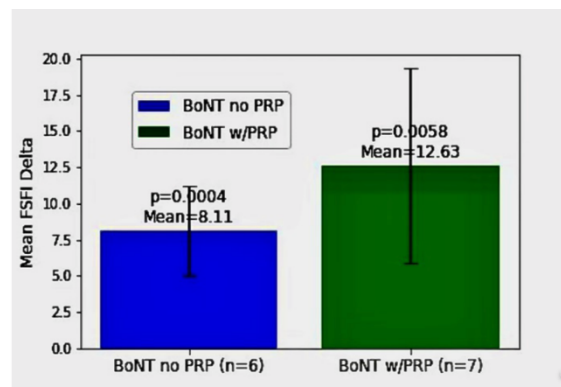
## What Is Possible with the Clitoxin® Procedure?

One of the problems with doing studies with female sex is that there's not an objective way to measure the results.<sup>39</sup> The female sexual function index is one proven way the sexual response is measured in women.

For comparison, if you're doing a study of a man's Peyronie's disease (his bent erection), you can measure that with a 10-cent protractor from the office supply store. If you're measuring erectile firmness, that's measurable, but to measure a woman's satisfaction, you can't measure that objectively. So, surveys are done, and the female sexual function index is one of the two or three most relied upon measures of the results. It has scores for different domains and a total score.

Here's one of the charts demonstrating our results.

When we injected botulinum toxin into the clitoris, the mean female sexual function index improved by eight. When we added platelet-rich plasma



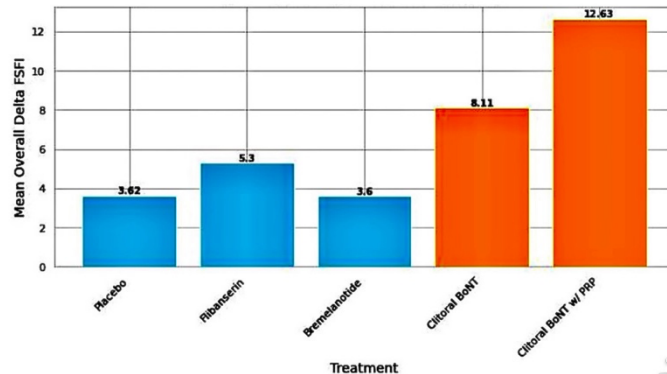
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(the primary part of the O-Shot® procedure) to the BoNT and injected the clitoris, the response went up to 12.

So, what does that mean, increasing the score by 8 with botulinum toxin to the clitoris by itself and 12 when it was added to platelet-rich plasma?

Here is a comparison.

A meta-analysis was done where the major treatments for sexual dysfunction in women were considered, and because the placebo effect is very strong in any study of female sexuality, the meta-analysis also looked at the average expected placebo effect for the treatment of female sexual dysfunction. Looking at Wellbutrin, flibanserin, and bremelanotide and what happened, the average placebo effect was 3.62. The average flibanserin effect improved by 5.3, and bremelanotide was 3.6 (about the average of the placebo in the other studies), but the placebo was less in the bremelanotide study.



To give you a reference of what those numbers mean, another number to remember is that you must raise the total score to above 26.5 for the women to be counted as not having a sexual dysfunction.

Most women who complain of sexual problems (to the point that they're distressed) show an average female sexual function index total of 20. The average score for women who are not complaining and who say sex is great, their average score is 30.

So, to get from the average presentation with sexual dysfunction that's disturbing (20), most women will have to go up by six or seven, and neither of the two main FDA-approved agents accomplishes that (they only raise the score by 3 or 5).

And neither of the FDA-approved, on-label drugs, flibanserin or bremelanotide, raise the score by the six or seven needed to suffer no dysfunction, and neither comes close to raising the score by the ten or more that would be required to go from the average of twenty in women with problems to the average of thirty with women with no problems.

In our study, the clitoral botulinum toxin alone bumped it by eight (enough to go from dysfunction to normal function), and when we added platelet-rich plasma (PRP) to the botulinum toxin, it raised the average score by twelve—*enough to take a woman from the average score seen with those suffering sexual dysfunction to that seen in women who are loving sex.*

That means it was such a robust response that you could use the other two, flibanserin or bremelanotide, as the placebo and still show a statistical benefit from the Clitoxin® procedure (if these numbers are borne out in future studies).

*In some women, BoNT injected into the clitoris could, if combined with platelet-rich plasma, take them from the average of 20 to greater than 30; there is nothing else that has been shown in any study to raise the total female sexual function index by that much.*

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*Part of the reason that multiple modalities are recommended in treating sexual dysfunction in women, even the shotgun approach where many things are used at the same time, sometimes without regard to the system's analysis, is that knowing there is not one therapy that has been shown to move people that far on the scale, there is the hope of an additive or synergistic effect by using multiple therapies that will bring women up the level of thirty.*

This idea, *Clitoxin® (injecting botulinum toxin in a very specific way into the clitoris), will not work if performed incorrectly.* But if it's done in a specific way, then our study shows the possibility of successful monotherapy for some women suffering sexual dysfunction.

### **Clitoxin® is a Non-FDA Approved, Off-Label Treatment**

This is an off-label, non-FDA-

approved use of botulinum toxin. So, let's talk about what that means.

The status of non-FDA-approved does not mean it's not supported by research and is not commonly used.<sup>51 52</sup> There are many supportive ideas about using botulinum toxin to help the three ways we just talked about: the autonomic nervous system, help with wound healing, dating back to the 1950s, help with vasodilatation or relaxation of smooth muscle. That's well known. It just wasn't obvious that it might be used in the clitoris.

But let's explore this further: 21 to 31% of all prescriptions are written for non-FDA-approved, off-label uses.<sup>53</sup>

That means around one in four prescriptions of the millions written daily are used off-label.

In one study, 90% of the children in the hospital received at least one off-label prescription. That's 90%, 9 out of 10 children in the hospital received at least one prescription during the hospitalization that was an off-label, non-FDA-approved use of the drug.<sup>54</sup>

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## Female Sexual Dysfunction and the Clitoxin® Procedure

### Why So Many Off-Label Prescriptions?

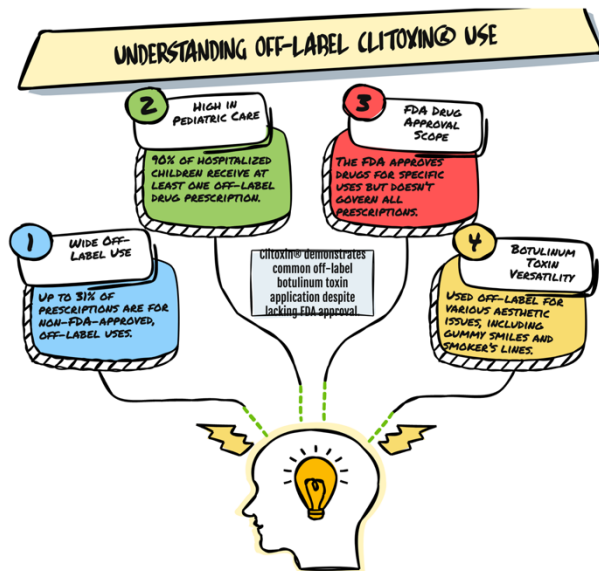
The FDA governs the approval of drugs and the advertisement of drugs by the manufacturer of the drug. They also govern devices, and we need the FDA. They help confirm that a drug is safe, the side effects are known, and the risks are understood.

The FDA also limits the manufacturers, the pharmaceutical companies, to only advertising the use of a drug for what it was shown (to the satisfaction of the FDA) to help. But that does not mean the FDA governs every prescription written—far from it.

They have nothing to do with the way surgeries are done. They have nothing to do with the way doctors practice medicine except regarding what I just told you.<sup>55 56</sup>

### The Off-Label Use of Botulinum Toxin for the Past Two Decades

Back to botulinum toxin, it's used millions of times per year—off-label. But why so many off-label prescriptions?



For example, botulinum toxin is used off-label for all these problems: smoker's lines, bruxism, crow's feet, gummy smile, platysma bands, down-turned corners of the mouth, and dimpled chin.<sup>57</sup> Just think about the gummy smile and the bunny lines alone that it's used for or take smokers lines, millions of times per year, arguably less serious indications than using it to help sexual function, and all of these uses are completely and totally off-label and not approved for that use by the FDA.

Thankfully, because botulinum has been used millions of times yearly for two decades, we have a good safety record for its use in women of childbearing age.

But forget botulinum toxin for now. Why are there so many off-label prescriptions?

Well, there are several.

### Orphan Indications and Why Pharmaceutical Companies Choose NOT to Seek FDA Approval for a Drug—Even When They Know It Works.

Some populations are difficult to study because of legal and risk problems.

For example, children are developing. There is a huge risk in giving drugs to children for fear of what might happen to them in the future. Women of childbearing age must worry about what will happen if they get pregnant while taking the drug. Because of these worries, pharmaceutical companies realize the low possibility of profit from the drug because the massive expense and risk of doing the studies to



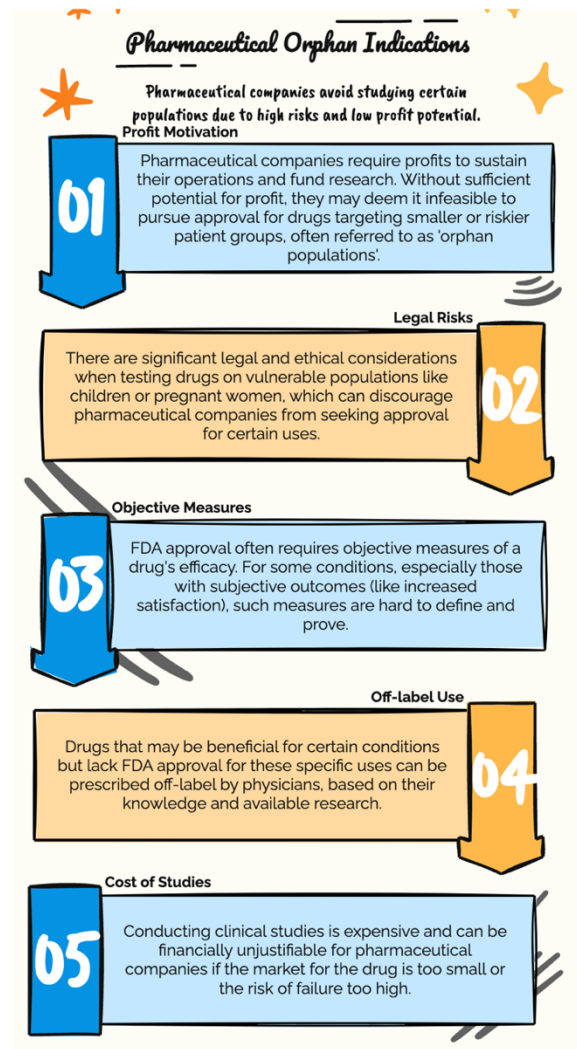
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reach on-label status make it impossible to reach FDA approval for the drug and remain in business. This situation does not signal malintent, only economic impossibility.

These are called an “*orphan population*” since pharmaceutical companies avoid doing studies on drugs to help them.<sup>52</sup>

The other factor that causes pharmaceutical companies to avoid research is problems with a hard-to-prove success goal. For example, with sexual dysfunction in women, for the drug to gain on-label, FDA-approved status by the FDA, the companies must prove that a drug improves satisfaction—proving only improved arousal or orgasm is not sufficient.<sup>52</sup>

Remember, there's no ruler to measure this objectively. So if she, for example, improves her libido, but



her lover is unable to keep pace with her, and she becomes frustrated and less satisfied, maybe she still has orgasms, but she doesn't have as many as she wants, and she's less satisfied, in that case, if other women had the same response, that drug would not be approved because her satisfaction went down. That is a very high bar, a very high bar, so high it becomes an “*orphan indication.*”

What I just told you about orphan indications and populations is a fact. What I'm about to tell you is an opinion: I think that that is why you will probably never see an on-label use of testosterone in women, even though testosterone is prescribed millions of times per year to help women with their sexual function and other problems. But there is no FDA-approved formula for testosterone for women, and probably never will be.

It's completely off-label the millions of times it's written every year, and men have multiple FDA-approved forms of testosterone because you only must prove that their penis gets hard (objective measure), which is much easier to do than to prove that a woman becomes more satisfied (a subjective psychological measure). That's objective versus subjective measurement. To push it even more into the orphan category, subjective measurement measures something that's so multifactorial it discourages the pharmaceutical companies from doing the studies. It was heroic and almost miraculous that flibanserin (Addyi®) was ever

approved because of the problems we discussed. It was abandoned because of such problems by the first company that had the drug, and another company (Sprout Pharmaceuticals) took it up and eventually pushed it to approval. It's a useful drug.

*Both flibanserin (only on-label and FDA-approved for premenopausal women) and bremelanotide are useful, but remember, neither of those drugs directly affects the female genitalia.* They're psych drugs, and their effects don't, on average, increase female sexual function the

## Female Sexual Dysfunction and the Clitoxin® Procedure

six to seven needed (on average) to go from dysfunction to function. Remember, flibanserin (in the studies) only improved on the average of one extra sexual encounter per month—not per week, per month.

### How Do the Pharmaceutical Companies Deal with Orphans?

The pharmaceutical companies must make a profit, or they cannot make any of our drugs. They must do research, and that takes profit. Even government-funded research is funded by taxes on someone's profit. Charities are supported by donations from someone who made a profit. There must be a surplus for businesses and governments to operate. Profit is surplus, and surplus keeps things rolling; deficits lead to collapse. So, the companies are not ill-intentioned; they must avoid collapse.

So, when an orphan indication arises (where proving its usefulness is beyond possibility without losing so much money that it just can't even be brought to market), the company sometimes recognizes that the prescriptions are being written (based on research and common practice) but loses the motivation to do the research.

For example, consider botulinum toxin for frown lines; the number elevens—botulinum toxin is brought to market, and the company secures on-label approval by the FDA for that indication. Now, it's approved but not for bruxism, but doctors have done studies that show it helps with headaches from bruxism. It's approved for migraine but not for grinding your teeth. But then doctors publish the research, show that it helps, and use it for bruxism. Now, the pharmaceutical company can be disincentivized to spend the money for FDA approval for bruxism. They have no further need to prove that indication because it's already on the market, the research is robust, and physicians are already writing prescriptions for it, so it remains an orphan, as in it never sustains the research dollars and effort that is required to make it FDA approved for that indication.

So, you may ask, "If you're going to use botulinum toxin to help with sex in women, is it safe?"

The same cautions and warnings that apply to the use of BoNT for cosmetic use, vaginismus, and bladder spasm would apply here: the woman should not be pregnant so that you don't have to worry about harming the unborn. It should not be used if the woman has a neurological disease like myasthenia gravis.

However, BoNT has been used in women of childbearing age with a very low complication rate for two decades, and it has also been routinely used millions of times per year *at three times the dosage (150 to 200 units for migraines) that we used in our study for the treatment of female sex problems (50 units)*.

And it has been used for two decades, with few complications, in the female genitalia, in the vagina, around Hart's line, around the urethra for vulvodynia and bladder spasm. It's been used in the bladder using a scope, running fiber-optic light through the urethra to inside the bladder, and injecting the bladder wall (not a fun thing to receive).

Further, the actual toxic dose of botulinum toxin, given intravenously if you just wanted to intentionally poison somebody with the usual concentration of cosmetic botulinum toxin, then the toxic dose is about \$150,000 worth.<sup>58 59</sup> A very tiny fraction of this toxic dose is used for common treatments like cosmetic use, bladder spasms, and bruxism.

### Serious Warning

## Female Sexual Dysfunction and the Clitoxin® Procedure

People are using non-FDA-approved forms of counterfeit botulinum toxin that they buy from cheap suppliers in other countries. That is dangerous and unethical. If you look at the people who have been hurt with the dosages that we're discussing (50 to 150 units), with genuine botulinum toxin from reputable FDA-governed suppliers, the incidence of serious sequelae is 1 in *millions*. BoNT is even used in children with cerebral palsy with muscle spasms of the back and legs at much higher doses with few complications.

The number of people with serious problems is less than one in millions. But only when it's bought from FDA-governed manufacturers. Physicians in the US should come from legitimate suppliers (Merz for Xeomin). If your provider is buying it through the mail from overseas, you are at great risk.

And it's even more disturbing because there is no medical board that governs the injection of BoNT. I know you'll see in the news, and you'll see online that botulinum toxin should only be done by a dermatologist or a plastic surgeon. But when you go to the dermatologist or the plastic surgeon's office, the nurse often injects the BoNT. Unless something has changed recently, there are no medical board tests on botulinum injections, cosmetic injections, or cosmetic fillers. It's surprising when you think about it since millions of doses are done yearly, but the last I checked, even with a plastic surgery residency, there is no testing on the cosmetic use of BoNT.

### What to Do?

So, how do you find the right person to provide the Clitoxin® procedure?

The short answer is that only those providers listed on the following website are licensed to do the procedure: [Clitoxin.com](http://Clitoxin.com).

But what determines who is listed there as a licensed provider?

First, there should be someone with the proper license to inject botulinum toxin, which varies considerably from state to state. Some states allow nurses to practice medicine independently without MD supervision (cardiology, endocrinology, cosmetic botulinum toxin, everything).<sup>1</sup> Some states demand an MD or a DO even to inject cosmetic BoNT<sup>1</sup>; some require a nurse practitioner degree, and some require an RN.

So, the requirements to inject BoNT in general widely differ. However, the injector should first be licensed in that state, according to the state's requirements where treatment takes place, to do the injections.

Also, and just as importantly, the injector should understand the anatomy of what they're injecting and the science of what they are treating. You've got RNs that give chemotherapy. You have RNs that do dialysis, RNs that do dialysis, which can cause death. RNs do home dialysis, and RNs do home chemotherapy.

So, an RN can inject something, assuming she's licensed in her state, if she understands the anatomy. If an RN can give chemotherapy and put in a Foley catheter, and she practices in a state that will license her, she can inject BoNT. A Foley catheter is much more dangerous than injecting botulinum toxin at the doses that we used in our study. But she should be licensed. She should have a license that allows her to inject botulinum toxin in her state, and she should be getting her botulinum toxin from her country.

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<sup>1</sup> For example, Alabama does not allow a nurse or nurse practitioner to inject cosmetic botulinum toxin; the injector must have an MD or DO degree.

## Female Sexual Dysfunction and the Clitoxin® Procedure

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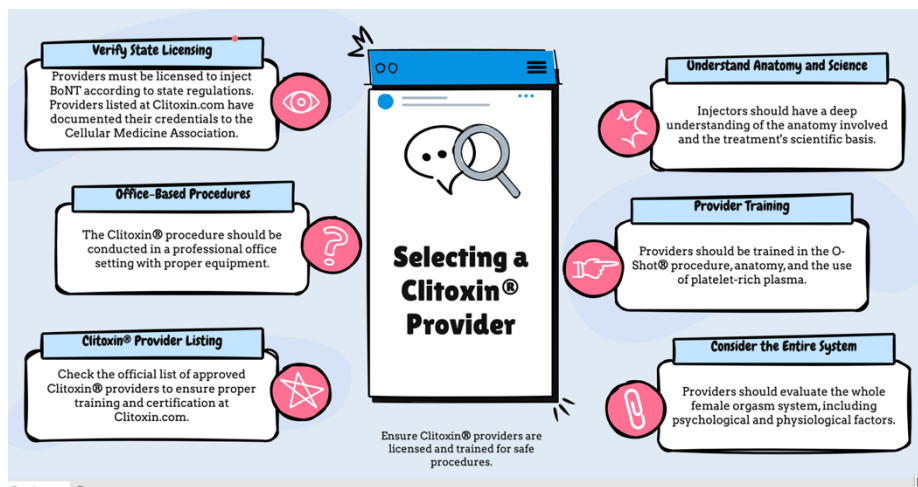
*Only those listed on the following website are licensed to do the procedure:  
[Clitoxin.com](http://Clitoxin.com)*

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So, when you see the news reports about something happening outside of an office, it's not the lack of an office that's to blame. Again, we commonly do home chemotherapy. It's just that oftentimes, if you have some fly-by-night person injecting BoNT, they're not even licensed to use botulinum toxin, but they bought it cheaply online from another country, and now they're having a clandestine party in somebody's house because they do not have the license to have an office, and they inject corrupted, highly concentrated botulinum, toxin the wrong way, and then somebody gets hurt.

So, cosmetic BoNT can be done outside the office, but the Clitoxin® procedure should not be done outside the office—it should be done in the office. The Clitoxin® procedure involves more than cosmetic BoNT and will require proper lighting and other supplies unavailable outside the office.

So, if you want the Clitoxin® procedure done, you should ensure whoever does it is listed as one of our providers.



I'm sure others will inject the clitoris with BoNT in their own way, better or worse. But before being listed on the Clitoxin® provider website, providers must have first demonstrated they understand how to do the O-Shot® procedure, understand the anatomy, and understanding how to

use platelet-rich plasma in the vagina, and then they have to demonstrate they understand the use of botulinum toxin and that understanding is documented as well as their license; then they may be added to our provider list.

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*There are no perfect procedures, and there's always the choice not to be treated at all or to be treated with something else or in another way.*

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*The complications from any procedure can be unexpected and severe. However, we think that the results of our study are promising, and there is reassurance in the safety of two decades of using botulinum toxin millions of times in women of childbearing age and using it even in the female genitalia and the strong science showing that the autonomic nervous system does play a critical role in the sexual function in regards to the arousal center and the massive autonomic nervous system innervating the clitoris through the inferior hypogastric complex—all of that together with the research showing that botulinum toxin relaxes the smooth muscle to increase blood flow*

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*to increase engorgement of the clitoris and can result in new nerves, neovascularization, collagenesis, and neurogenesis—Clitoxin® could be a possible treatment for some women.*

Also, even if your provider offers the Clitoxin® procedure, they should consider the whole female orgasm system (or have someone else in the office or another office think about the female orgasm system). All parts of the female orgasm system should be considered: for example, social, hormonal, neurological (autonomic and somatic), psychological, cardiovascular, and other drugs that may be affecting sexuality.

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*Giving every woman a clitoris shot to help sex  
is not acceptable.*

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I hope that's helpful. I look forward to more research confirming (or disproving) our pilot study. So far, the word from our providers has been too remarkable to even talk about.

Oftentimes, we hear that women find themselves more easily aroused and say, "This must be what it's like to be a teenage boy."

Not that they're aroused all the time, they're not aroused all the time; but they find it easier to become aroused and to have orgasms. And if that helps any number of people without serious sequelae, that's a very good thing.

If you think this may help you or someone you love, I hope you will discuss the possibility with your chosen provider and your current primary care physician or gynecologist.

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<sup>i</sup> The states that allow full practice authority for Nurse Practitioners—meaning they can evaluate patients, diagnose, order and interpret diagnostic tests, and initiate and manage treatments, including prescribing medications, under the authority of the state board of nursing without requiring a supervising physician—are as follows: Alaska, Arizona, Colorado, Connecticut, Delaware, Hawaii, Idaho, Maine, Maryland, Minnesota, Montana, Nebraska, Nevada, New Hampshire, New Mexico, North Dakota, Oregon, Rhode Island, South Dakota, Vermont, Washington, Wyoming.